IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
PATENT APPLICATION EXAMINING OPERATIONS

Appl. No.	: 09/742,785	Confirmation No. 8464
Applicant	: Curatolo et al.	
Filed	: December 20, 2000	
Title	: Pharmaceutical Compositions Providing Enhanced Drug Concentrations	
TC/A.U.	: 1618	
Examiner	: Fubara, Blessing M.	
Docket No.	: 0003.0565/PC10755A	
Customer No.	: 00152	

DECLARATION OF JAMES NIGHTINGALE UNDER RULE 131

1. I am a co-inventor of the invention described and claimed in the above-identified application and of Curatolo et al. US Patent No. 6,548,555 (the '555 patent) and am thoroughly familiar with the subject matter of the instant application and the '555 patent.

2. Attached hereto as Exhibit A is a copy of a lab notebook pertaining to the invention disclosed and claimed in the instant application. Specifically, Exhibit A records the details of an experiment to determine the effect on a drug's solubility of forming a highly soluble salt of the crystalline form of the drug and mixing dry particles of the salt form with dry particles of hydroxypropyl methyl cellulose acetate succinate (HPMCAS), known in the pharmaceutical arts as a triturate. The drug tested is a proprietary antipsychotic agent having an aqueous solubility of less than 0.01 mg/mL at pH 1 to 8 that is owned by Pfizer, Inc. and the drug's internal designation has been redacted to preserve confidentiality.

3. In the experiment, the solubility of three forms of the drug was tested: (1) crystalline drug alone; (2) a triturate of the crystalline mesylate of the drug and HPMCAS; and (3) a solid amorphous spray-dried dispersion of the drug and HPMCAS. Dissolution testing was conducted at 37°C in the same manner described in paragraphs [0122] and [0123] of the published version (US 2002/0006443) of the instant application.

The details of the dissolution tests for the three drug forms and the results of the tests are set out in a printout of a computerized spread sheet attached hereto as Exhibit B. As is apparent from the Results table and graph in Exhibit B, the triturate composition (BRI Ref. No. 1457-115b) exhibited a vast improvement in the drug's C_{max}, AUC90 and 20 hour concentration relative to crystalline drug alone. All the formulation work and dissolution testing reflected in Exhibits A and B were conducted in 1997, or well before February 9, 1999 (the lab book numbers and the dates on Exhibits A and B have been redacted to preserve confidentiality).

4. At the time the claimed invention of the application was made, the subject matter of both the claimed invention and of the '555 patent were owned by Pfizer, Inc. or subject to obligation of assignment to Pfizer Inc.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Dated this 29 day of November, 2010

James A. S. Nightingale

TITLE Dissolution of [redacted] Trit vs [redacted] Sprayed Project No. 957-003 Book No. [redacted]

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(A) Triturated 1:9 [redacted] : HPMCAS-HF (Lot# 111079)
11.6 mg [redacted]
109.9 mg HF

(B) Triturated 1:9 [redacted] : HPMCAS-HF (Lot# 111079)
12.0 ~~+5+~~ mg [redacted]
107.5 mg HF

1atb crystalline free base 0.18mg
2atb crystalline mesylate 0.18mg
3atb 1:9 freebase/HF (1465-101) 1.8mg
4atb 1:9 mesyl/HF (1465-61E)
5atb Trit 1:9 Free b/HF (1457-115A)
6atb Trit 1:9 mes/HF (1457-115B)
7atb 1:9 Free base/AC (1465-101)
8atb 1:9 Mesylate/HF (1465-61E)

[redacted] Stk1
0.824mg in 50mL
- 16.5 ppm
- 8.25 ppm
- 4.13 ppm
- 1.65 ppm

[redacted] Stk1
0.853 mg in 50mL
17.06 ppm
8.53 ppm
4.27 ppm
1.71 ppm

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Witnessed & Understood by me. | Date | Invented by [redacted] | Date [redacted]

Exhibit A
Nightingale Declaration

Title	**Dissolution of [redacted] in MFDS**
Drug	0.18 mg crystalline [redacted] 1.8 mg 1:9 [redacted]:HPMCAS-HF dispersion(BRI Ref. No. 1485-61e) 1.8 mg 1:9 [redacted]:HPMCAS-HF triturated(BRI Ref. No. 1457-115b)
Receptor Solution	1.8 mL NaTC-POPC in PBS, pH 6.5, 290 mOsm/kg
Date Performed	[redacted] **Notebook** [redacted]
Operator	KEC
Comments	All work done in a 37C temperature controlled box.

Results

Sample	C_{max} (µg/mL)	AUC90 (min*µg/mL)	20hr Conc. (µg/mL)	Theor C_{max} (µg/mL)
1485-61e	17	1,200	5	80.9
[redacted]	0	0	0	80.3
1457-115B	11	823	6	80.3

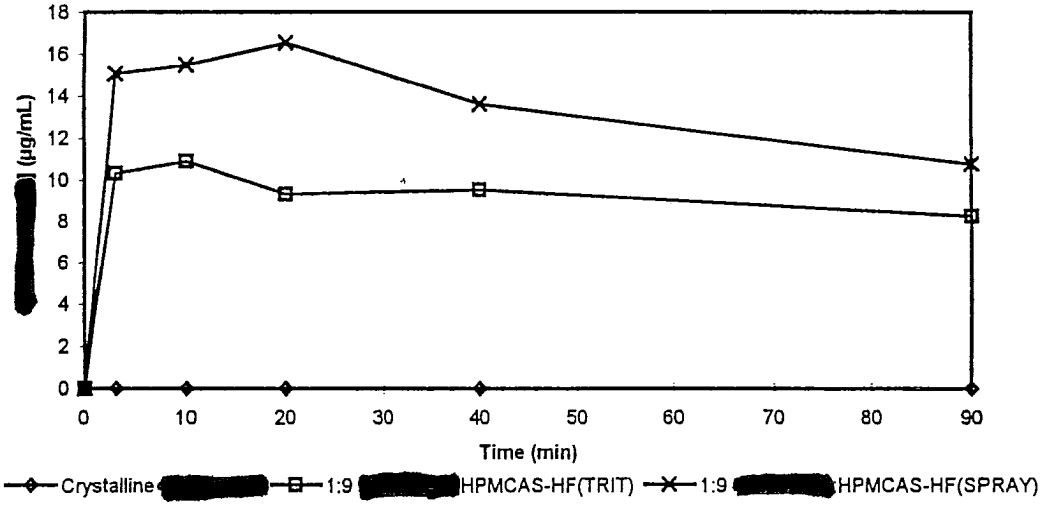

Exhibit B
Nightingale Declaration